SEQUENCE LISTING

| (1) GENERAL | INFORMATION: |
|-------------|--------------|
|-------------|--------------|

5

(i) APPLICANT:

(A) NAME: PEPTIDE THERAPEUTICS LIMITED

(B) STREET: 100 Fulbourn Road

(C) CITY: Cambridge

10 (D) STATE: not applicable

(E) COUNTRY: United Kingdom

(F) POSTAL CODE (ZIP): CB1 9PT

(ii) TITLE OF INVENTION: ATTENUATED BACTERIA USEFUL IN VACCINES

15

(iii) NUMBER OF SEQUENCES: 6

(iv) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk

20 (B) COMPUTER: IBM PC compatible

(C) OPERATING SYSTEM: PC-DOS/MS-DOS

(D) SOFTWARE: PatentIn Release #1.0. Version #1.30 (EPO)

(v) CURRENT APPLICATION DATA:

25 APPLICATION NUMBER:

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 1690 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

35 (ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:



(A) ORGANISM: aroC of E.coli

(ix) FEATURE:

(A) NAME/KEY: CDS

5 (B) LOCATION: 492..1562

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

| | GTCGACGCGG TGGATATCTC TCCAGACGCG CTGGCGGTTG CTGAACAGAA CATCGAAGAA | 60 |
|----|---|-----|
| 10 | CACGGTCTGA TCCACAACGT CATTCCGATT CGTTCCGATC TGTTCCGCGA CTTGCCGAAA | 120 |
| | GTGCAGTACG ACCTGATTGT CACTAACCCG CCGTATGTCG ATGCGAAGAT ATGTCCGACC | 180 |
| | TGCCAAACAA TACCGCCACG AGCCGGAACT GGGCCTGGCA TCTGGCACTG ACGGCCTGAA | 240 |
| | ACTGACGCGT CGCATTCTCG GTAACGCGGC AGATTACCTT GCTGATGATG GCGTGTTGAT | 300 |
| | TTGTGAAGTC GGCAACAGCA TGGTACATCT TATGGAACAA TATCCGGATG TTCCGTTCAC | 360 |
| 15 | CTGGCTGGAG TTTGATAACG GCGGCGATGG TGTGTTTATG CTCACCAAAG AGCAGCTTAT | 420 |
| | TGCCGCACGA GAACATTTCG CGATTTATAA AGATTAAGTA AACACGCAAA CACAACAATA | 480 |
| | ACGGAGCCGT G ATG GCT GGA AAC ACA ATT GGA CAA CTC TTT CGC GTA ACC | 530 |
| | Met Ala Gly Asn Thr Ile Gly Gln Leu Phe Arg Val Thr | |
| | 1 5 10 | |
| 20 | | |
| | ACC TTC GGC GAA TCG CAC GGG CTG GCG CTC GGC TGC ATC GTC GAT GGT | 578 |
| | Thr Phe Gly Glu Ser His Gly Leu Ala Leu Gly Cys Ile Val Asp Gly | |
| | 15 20 25 | |
| | | |
| 25 | GTT CCG CCA GGC ATT CCG CTG ACG GAA GCG GAC CTG CAA CAT GAC CTC | 626 |
| | Val Pro Pro Gly Ile Pro Leu Thr Glu Ala Asp Leu Gln His Asp Leu | |
| | 30 35 40 45 | |
| | | |
| | GAC CGT CGT CGC CCT GGG ACA TCG CGC TAT ACC ACC CAG CGC CGC GAG | 674 |
| 30 | Asp Arg Arg Pro Gly Thr Ser Arg Tyr Thr Thr Gln Arg Arg Glu | |
| | 50 55 60 | |
| | | |
| | CCG GAT CAG GTC AAA ATT CTC TCC GGT GTT TTT GAA GGC GTT ACT ACC | 722 |
| | Pro Asp Gln Val Lys Ile Leu Ser Gly Val Phe Glu Gly Val Thr Thr | |
| 35 | 65 70 75 | |
| | | |
| | GGC ACC AGC ATT GGC TTG TTG ATC GAA AAC ACT GAC CAG CGC TCT CAG | 770 |

WO 99/49026 PCT/GB99/00935

| | Gly | ' Thr | Ser 80 | | Gly | Leu | Leu | Ile 85 | Glu | Asn | Thr | Asp | G1n 90 | _ | Ser | Gln | |
|----|------------|-------|-------------------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|------|
| 5 | | | AGT Ser | | | | | | | | | | His | | | | 818 |
| 10 | | Tyr | GAA G1u | | | | | | | | | | | | | | 866 |
| 15 | | | GCC Ala | | | | | | | | | | | | | | 914 |
| 13 | | | TAT Tyr | | | | | | | | | | | | | | 962 |
| 20 | | | ATG Met 160 | | | | | | | | | | | | | | 1010 |
| 25 | | | AAT Asn | | | Phe | | | | | Asp | | | | | | 1058 |
| 30 | | | TTG Leu | | Arg | | | | | | | | | | | | 1106 |
| 35 | | | ACC Thr | Val | | | | | Val | | | | | Gly | | | 1154 |
| | GTC Val | | GAC Asp | | | | | | | | | | | | | | 1202 |



| WU | 77/4 | 7020 | , | | | | | | | | | | | | | | | |
|----|------|------|-------|-----|-------|-------|------|-------|-------|-------|-------|-------|-------|-------|-------|----------------|------|------|
| | | | | 225 | | | | | 230 | | | | | 235 | | | | |
| | AAC | GCG | GTG | AAA | GGC | GTG | GAA | ATT | GGC | GAC | GGC | ПТ | GAC | GTG | GTG | GCG | 125 | 0 |
| | Asn | Αla | Val | Lys | Gly | Va1 | Glu | Пe | G1 y | Asp | Gly | Phe | Asp | ۷a٦ | Val | Ala | | |
| 5 | | | 240 | | | | | 245 | | | | | 250 | | | | | |
| _ | | | | | | | | | | | | | | | | | | |
| | CTG | CGC | GGC | AGC | CAG | AAC | CGC | GAT | GAA | ATC | ACC | AAA | GAC | GGT | ттс | CAG | 129 | 8 |
| | Leu | Arg | Gly | Ser | Gln | Asn | Arg | Asp | Glu | Пe | Thr | Lys | Asp | G1 y | Phe | Gln | | |
| | | 255 | | | | | 260 | | | | | 265 | | | | | | |
| 10 | | | | | | | | | | | | | | | | | | |
| | AGC | AAC | CAT | GCG | GGC | GGC | ATT | СТС | GGC | GGT | ATC | AGC | AGC | GGG | CAG | CAA | 134 | 16 |
| | Ser | Asn | His | Ala | Gly | G1 y | Пe | Leu | Gly | Gly | Ile | Ser | Ser | G1 y | Gln | Gln | | |
| | 270 | | | | | 275 | | | | | 280 | | | | | 285 | | |
| | | | | | | | | | | | | | | | | | | |
| 15 | ATC | ATT | GCC | CAT | ATG | GCG | CTG | AAA | CCG | ACC | TCC | AGC | ATT | ACC | GTG | CCG | 139 | 94 |
| | Пe | Ile | Ala | His | Met | Ala | Leu | Lys | Pro | Thr | Ser | Ser | Пe | Thr | ۷a۱ | Pro | | |
| | | | | | 290 | | | | | 295 | | | | | 300 | | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | AAA | 14 | 42 |
| 20 | Gly | Arg | Thr | Ile | Asn | Arg | Phe | Gly | Glu | Glu | Va1 | Glu | Met | Ile | Thr | Lys | | |
| | | | | 305 | | | | | 310 | | | | | 315 | | | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | GAA | 14 | 90 |
| | G1 y | Arg | His | Asp | Pro | Cys | Va1 | Gly | Ile | Arg | Ala | Val | Pro | Ile | Ala | Glu | | |
| 25 | | | 320 | | | | | 325 | • | | | | 330 | I | | | | |
| | | | | | | | | | | | | | | | | | 1.5 | 20 |
| | | | | | | | | | | | | | | | | GGC | 15 | 38 |
| | Ala | Asr | ı Ala | G1y | / Asp | Arg | Phe | Asn | ı Gly | Ser | Pro | | | Ala | Thr | · G1y | | |
| | | 335 | • | | | | 340 |) | | | | 345 |) | | | | | |
| 30 | | | | | | | | | | | 1 | | | | -0447 | | 1.5 | ·02 |
| | | | | | | | | | TAT | TCCA | ACGC | TGGT | AAA/ | VAA T | GAA | FAAAA C | 15 | 92 - |
| | A٦a | Ly: | s Cys | Arg | g Cys | 61u | | * | | | | | | | | | | |
| | 350 |) | | | | 355 | 5 | | | | | | | | | | | |
| | | | | | | | | | | | | | 2004 | 2004 | CCC | ~~ ~ ~~ | ۸ 14 | 552 |
| 35 | CGO | CGAT | TGCG | CTG | CTGG | CTC 1 | GCTT | rgcc/ | AG T | AGCG(| CCAG(| . CT(| aGCA(| AEUSE | CGC | CGTGGC | W 10 | 552 |

AAAAATAACC CAACCTGTGC CGGGTAGCGC CAAATCGA



(2) INFORMATION FOR SEQ ID NO: 2:

| (i) | SEQUENCE | CHARACTERISTICS |
|-----|----------|-----------------|
|-----|----------|-----------------|

(A) LENGTH: 356 amino acids

(B) TYPE: amino acid(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Met Ala Gly Asn Thr Ile Gly Gln Leu Phe Arg Val Thr Thr Phe Gly
1 5 10 15

Glu Ser His Gly Leu Ala Leu Gly Cys Ile Val Asp Gly Val Pro Pro 20 25 30

Gly Ile Pro Leu Thr Glu Ala Asp Leu Gln His Asp Leu Asp Arg Arg
35 40 45

Arg Pro Gly Thr Ser Arg Tyr Thr Thr Gln Arg Arg Glu Pro Asp Gln
50 55 60

Val Lys Ile Leu Ser Gly Val Phe Glu Gly Val Thr Thr Gly Thr Ser
25 65 70 75 80

Ile Gly Leu Leu Ile Glu Asn Thr Asp Gln Arg Ser Gln Asp Tyr Ser 85 90 95

30 Ala Ile Lys Asp Val Phe Arg Pro Gly His Ala Asp Tyr Thr Tyr Glu 100 105 110

Gln Lys Tyr Gly Leu Arg Asp Tyr Arg Gly Gly Gly Arg Ser Ser Ala 115 120 125

Arg Glu Thr Ala Met Arg Val Ala Ala Gly Ala Ile Ala Lys Lys Tyr
130 135 140

| | Leu / | Ala | G1u | Lys | Phe | Gly 150 | lle | G1u | lle . | Arg | Gly 155 | Cys | Leu | Thr | | Met 160 |
|----|------------|-------------------------|--------------|--------------|------------|------------|------------|------------|------------|------------|------------|-------------|--------------|------------|-------------|--------------|
| 5 | Gly | Asp | Ile | Pro | Leu 165 | Asp | Пе | Lys | Asp | Trp 170 | Ser | Gln | Val | G1 u | G1 n 175 | Asn |
| | Pro | Phe | Phe | Cys 180 | Pro | Asp | Pro | Asp | Lys 185 | Ile | Asp | Ala | Leu | Asp 190 | Glu | Leu |
| 10 | Met | Arg | Ala 195 | Leu | Lys | Lys | Glu | Gly 200 | Asp | Ser | Ile | G1 y | A1a 205 | Lys | Val | Thr |
| | Val | Val 210 | | Ser | Gly | Val | Pro 215 | Ala | Gly | Leu | Gly | G1u 220 | Pro | Val | Phe | Asp |
| 15 | Arg 225 | Leu | Asp | Ala | Asp | Ile 230 | Ala | His | Ala | Leu | Met 235 | | Пе | Asn | Ala | Val 240 |
| 20 | Lys | Gly | √ Val | Glu | Ile 245 | Gly | Asp | Gly | Phe | Asp 250 | | Val | Ala | Leu | Arg 255 | |
| | Ser | Glr | n Asr | n Arg 260 | | Glu | Ile | . Thr | Lys 265 | | Gly | , Phe | Gln | Ser 270 | | His |
| 25 | Ala | Gly | y G1: 27! | | e Lei | ı Gly | Gly | / Ile | | · Sei | r Gly | / Glr | o G1r 289 | | : Ile | e Ala |
| | His | s Me ⁻ 29 | | a Le | u Ly | s Pro | 7hi 29! | | · Sei | ^ I1 | e Thi | r Va 300 | | GT: | y Arg | g Thr |
| 30 | I)(| | n Ar | g Ph | e G1 | y G1: | | u Va | l Gl | u Me | t II | | r Ly | s G1 | y Ar | g His 320 |

35 Asp Pro Cys Val Gly Ile Arg Ala Val Pro Ile Ala Glu Ala Asn Ala

325

330



| Gly | Asp | Arg | Phe | Asn | Gly | Ser | Pro | Val | Thr | Ala | Thr | Gly | Ala | Lys | Cys |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | | 340 | | | | | 345 | | | | | 350 | | |

| Arg | Cys | Glu | Asp | * |
|-----|-----|-----|-----|---|
| | | 355 | | |

(2) INFORMATION FOR SEQ ID NO: 3:

| (i) | SEQUENCE | CHARACTERISTICS: |
|-----|----------|------------------|

10 (A) LENGTH: 1713 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: DNA (genomic)

(vi) ORIGINAL SOURCE:

(A) ORGANISM: ompC of E.coli

20 (ix) FEATURE:

30

35

(A) NAME/KEY: CDS

(B) LOCATION: 491..1594

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

| | GTTAACAAGC | GTTATAGTTT | TTCTGTGGTA | GCACAGAATA | ATGAAAAGTG | TGTAAAGAAG | 60 |
|---|------------|------------|------------|------------|------------|------------|-----|
| | GGTAAAAAA | ACCGAATGCG | AGGCATCCGG | TTGAAATAGG | GGTAAACAGA | CATTCAGAAA | 120 |
| 1 | TGAATGACGG | TAATAAATAA | AGTTAATGAT | GATAGCGGGA | GTTATTCTAG | TTGCGAGTGA | 180 |
| | AGGTTTTGTT | TTGACATTCA | GTGCTGTCAA | ATACTTAAGA | ATAAGTTATT | GATTTTAACC | 240 |
| • | TTGAATTATT | ATTGCTTGAT | GTTAGGTGCT | TATTTCGCCA | TTCCGCAATA | ATCTTAAAAA | 300 |
| | GTTCCCTTGC | ATTTACATTT | TGAAACATCT | ATAGCGATAA | ATGAAACATC | TTAAAAGTTT | 360 |

PCT/GB99/00935 WO 99/49026 TAGTATCATA TTCGTGTTGG ATTATTCTGC ATTTTTGGGG AGAATGGACT TGCCGACTGA TTAATGAGGG TTAATCAGTA TGCAGTGGCA TAAAAAAGCA AATAAAGGCA TATAACAGAG GGTTAATAAC ATG AAA GTT AAA GTA CTG TCC CTG GTC CCA GCT CTG Met Lys Val Lys Val Leu Ser Leu Leu Val Pro Ala Leu CTG GTA GCA GGC GCA GCA AAC GCT GCT GAA GTT TAC AAC AAA GAC GGC Leu Val Ala Gly Ala Ala Asn Ala Glu Val Tyr Asn Lys Asp Gly AAC AAA TTA GAT CTG TAC GGT AAA GTA GAC GGC CTG CAC TAT TTC TCT Asn Lys Leu Asp Leu Tyr Gly Lys Val Asp Gly Leu His Tyr Phe Ser GAC AAC AAA GAT GTA GAT GGC GAC CAG ACC TAC ATG CGT CTT GGC TTC Asp Asn Lys Asp Val Asp Gly Asp Gln Thr Tyr Met Arg Leu Gly Phe AAA GGT GAA ACT CAG GTT ACT GAC CAG CTG ACC GGT TAC GGC CAG TGG Lys Gly Glu Thr Gln Val Thr Asp Gln Leu Thr Gly Tyr Gly Gln Trp GAA TAT CAG ATC CAG GGC AAC AGC GCT GAA AAC GAA AAC AAC TCC TGG Glu Tyr Gln Ile Gln Gly Asn Ser Ala Glu Asn Glu Asn Asn Ser Trp ACC CGT GTG GCA TTC GCA GGT CTG AAA TTC CAG GAT GTG GGT TCT TTC Thr Arg Val Ala Phe Ala Gly Leu Lys Phe Gln Asp Val Gly Ser Phe GAC TAC GGT CGT AAC TAC GGC GTT GTT TAT GAC GTA ACT TCC TGG ACC 35 Asp Tyr Gly Arg Asn Tyr Gly Val Val Tyr Asp Val Thr Ser Trp Thr

PCT/GB99/00935 WO 99/49026 GAC GTA CTG CCA GAA TTC GGT GGT GAC ACC TAC GGT TCT GAC AAC TTC Asp Val Leu Pro Glu Phe Gly Gly Asp Thr Tyr Gly Ser Asp Asn Phe ATG CAG CAG CGT GGT AAC GGC TTC GCG ACC TAC CGT AAC ACT GAC TTC ·Met Gln Gln Arg Gly Asn Gly Phe Ala Thr Tyr Arg Asn Thr Asp Phe TTC GGT CTG GTT GAC GGC CTG AAC TTT GCT GTT CAG TAC CAG GGT AAA Phe Gly Leu Val Asp Gly Leu Asn Phe Ala Val Gln Tyr Gln Gly Lys AAC GGC AAC CCA TCT GGT GAA GGC TTT ACT AGT GGC GTA ACT AAC AAC Asn Gly Asn Pro Ser Gly Glu Gly Phe Thr Ser Gly Val Thr Asn Asn GGT CGT GAC GCA CTG CGT CAA AAC GGC GAC GGC GTC GGC GGT TCT ATC Gly Arg Asp Ala Leu Arg Gln Asn Gly Asp Gly Val Gly Gly Ser Ile ACT TAT GAT TAC GAA GGT TTC GGT ATC GGT GGT GCG ATC TCC AGC TCC Thr Tyr Asp Tyr Glu Gly Phe Gly Ile Gly Gly Ala Ile Ser Ser Ser AAA CGT ACT GAT GCT CAG AAC ACC GCT GCT TAC ATC GGT AAC GGC GAC Lys Arg Thr Asp Ala Gln Asn Thr Ala Ala Tyr Ile Gly Asn Gly Asp CGT GCT GAA ACC TAC ACT GGT GGT CTG AAA TAC GAC GCT AAC AAC ATC Arg Ala Glu Thr Tyr Thr Gly Gly Leu Lys Tyr Asp Ala Asn Asn Ile - 610 TAC CTG GCT GCT CAG TAC ACC CAG ACC TAC AAC GCA ACT CGC GTA GGT Tyr Leu Ala Ala Gln Tyr Thr Gln Thr Tyr Asn Ala Thr Arg Val Gly TCC CTG GGT TGG GCG AAC AAA GCA CAG AAC TTC GAA GCT GTT GCT CAG

| | Ser | Leu | G1 y | Trp | Ala | Asn | Lys | Ala | Gln | Asn | Phe | Glu | Ala | Val | Ala | Gln | |
|-----|-------|------------|-------|---------|----------|--------|-----------|-------|-------|-------|---|---------|--------|-------|---|---|------|
| | | | | 630 | | | | | 635 | | | | | 640 | | | |
| | | | | | | | | | | | | | | | | | |
| | TAC | CAG | ттс | GAC | ттс | GGT | CTG | CGT | CCG | TCC | CTG | GCT | TAC | CTG | CAG | TCT | 1393 |
| 5 | | | Phe | | | | | | | | | | | | | | |
| J | | | 645 | • | | | | 650 | | | | | 655 | | | | |
| | | | | | | | | | | | | | | | | | |
| | ΔΔΑ | GGT | AAA | AAC | CTG | GGT | CGT | GGC | TAC | GAC | GAC | GAA | GAT | ATC | CTG | AAA | 1441 |
| | | | Lys | | | | | | | | | | | | | | |
| 10 | 2,3 | 660 | _, - | | | - 0 | 665 | • | , | · | | 670 | | | | | |
| 10 | | 000 | | | | | | | | | | | | | | | |
| | TAT | GTT | GAT | GTT | GGT | GCT | ACC | TAC | TAC | ттс | AAC | AAA | AAC | ATG | TCC | ACC | 1489 |
| | | | Asp | | | | | | | | | | | | | | |
| | 675 | Vai | ASP | • • • • | u., | 680 | • • • • • | | | | 685 | | | | | 690 | |
| 1 E | 6/5 | | | | | 000 | | | | | | | | | | | |
| 15 | TAC | CTT | CVC | TAC | ΔΔΔ | ΔTC | ΔΔC | CTG | CTG | GAC | GAC | AAC | CAG | TTC | ACT | CGT | 1537 |
| | | | | | | | | | | | | | | | | Arg | |
| | ıyr | Val | ASP | ı yı | 695 | | AJII | LCu | | 700 | | | | | 705 | | |
| | | | | | 053 | | | | | , , , | | | | | | | |
| 0.0 | 040 | CCT | | ATC | A A C | ACT | CAT | ۸۵۲ | ΔΤΟ | GTA | GCT | CTG | GGT | СТС | GTT | TAC | 1585 |
| 20 | | | | | | | | | | | | | | | | Tyr | |
| | ASP | Ald | ы | | | , ,,,, | vah | 7,31 | 715 | | ,,,, | | | 720 | | · | |
| | | | | 710 | , | | | | ,10 | | | | | | | | |
| | C 4 C | TT(| : TAA | тст | CCAT | TCA | TATO | CVV | 'ΔΔ - | :בפרר | TGCG | ig go | CCTT | П | - | | 1634 |
| 2.5 | | | | 101 | CUAI | IUA | IAIC | | | duoc | ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, | | | | | | |
| 25 | GIN | Phe | | | | | | | | | | | | | | | |
| | | | 725 |) | | | | | | | | | | | | | |
| | | - 0 | | 4000 | T. C. | | TCAC | · | ст то | CTCT | racto | · TT6 | CCAC | CGT | TCGC | CATGAGG | 1694 |
| | CAI | 1611 | HIL | AGC | 1 ACA | WA (| ICAC | 21111 | 1 10 | 20101 | IAC I | , , , , | 200110 | ,ou 1 | ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, | ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, | |
| | | | | 1000 | ~ 4 4 4- | r a | | | | | | | | | | | 1713 |
| 30 | AIA | | ACGT | ACG | | IA | | | | | | | | | | | |
| | | ; | | | | • | | | | | | | | | | | |
| | | | | ATTO! | א בסי | ם כבי | י זרי | NO. | 4. | | | | | | | | |
| | (2) | IN | FORM | 4 I TU | N PU | n 3El | ע זט | MO: | ٦. | | | | | | | | |
| | | | | | | E 01: | 4D 4 C | TEDT | CTIC | c. | | | | | | | |

(i) SEQUENCE CHARACTERISTICS:

35

(A) LENGTH: 367 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

| (ii) | MOLECULE | TYPE: | protein |
|------|----------|-------|---------|
|------|----------|-------|---------|

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

5

Met Lys Val Lys Val Leu Ser Leu Leu Val Pro Ala Leu Leu Val Ala 1 5 10 15

Gly Ala Ala Asn Ala Ala Glu Val Tyr Asn Lys Asp Gly Asn Lys Leu 10 20 25 30

Asp Leu Tyr Gly Lys Val Asp Gly Leu His Tyr Phe Ser Asp Asn Lys
35 40 45

15 Asp Val Asp Gly Asp Gln Thr Tyr Met Arg Leu Gly Phe Lys Gly Glu
50 55 60

Thr Gln Val Thr Asp Gln Leu Thr Gly Tyr Gly Gln Trp Glu Tyr Gln
65 70 75 80

20

Ile Gln Gly Asn Ser Ala Glu Asn Glu Asn Asn Ser Trp Thr Arg Val · 85 90 95

Ala Phe Ala Gly Leu Lys Phe Gln Asp Val Gly Ser Phe Asp Tyr Gly
100 105 110

Arg Asn Tyr Gly Val Val Tyr Asp Val Thr Ser Trp Thr Asp Val Leu
115 120 125

Pro Glu Phe Gly Gly Asp Thr Tyr Gly Ser Asp Asn Phe Met Gln Gln
130 135 140

Arg Gly Asn Gly Phe Ala Thr Tyr Arg Asn Thr Asp Phe Phe Gly Leu 145 150 155 160

35

Val Asp Gly Leu Asn Phe Ala Val Gln Tyr Gln Gly Lys Asn Gly Asn 165 170 175

| Pro | Ser | Gly | Glu | Gly | Phe | Thr | Ser | Gly | Val | Thr | Asn | Asn | Gly | Arg | Asp |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | | 180 | | | | | 185 | | | | | 190 | | |

- Ala Leu Arg Gln Asn Gly Asp Gly Val Gly Gly Ser Ile Thr Tyr Asp
 5 195 200 205
 - Tyr Glu Gly Phe Gly Ile Gly Gly Ala Ile Ser Ser Lys Arg Thr 210 215 220
- Asp Ala Gln Asn Thr Ala Ala Tyr Ile Gly Asn Gly Asp Arg Ala Glu 225 230 235 240
 - Thr Tyr Thr Gly Gly Leu Lys Tyr Asp Ala Asn Asn Ile Tyr Leu Ala 245 250 255
 - Ala Gln Tyr Thr Gln Thr Tyr Asn Ala Thr Arg Val Gly Ser Leu Gly
 260 265 270
- Trp Ala Asn Lys Ala Gln Asn Phe Glu Ala Val Ala Gln Tyr Gln Phe 20 275 280 285
 - Asp Phe Gly Leu Arg Pro Ser Leu Ala Tyr Leu Gln Ser Lys Gly Lys 290 295 300
- Asn Leu Gly Arg Gly Tyr Asp Asp Glu Asp Ile Leu Lys Tyr Val Asp 305 310 315 320
 - Val Gly Ala Thr Tyr Tyr Phe Asn Lys Asn Met Ser Thr Tyr Val Asp 325 330 335
 - Tyr Lys Ile Asn Leu Leu Asp Asp Asn Gln Phe Thr Arg Asp Ala Gly
 340 345 350
- Ile Asn Thr Asp Asn Ile Val Ala Leu Gly Leu Val Tyr Gln Phe * 35 355 360 365



| (2) | INFORMATION | FOR | SE ₀ | ID | NO: | 5 |
|-----|-------------|-----|-----------------|----|-----|---|

| (i) | SECLIENCE | CHARACTER IS | TTCS. |
|-----|-----------|---------------|-------|
| | JEVULITUL | CHAMO I FILLS | 1163. |

(A) LENGTH: 1808 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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(vi) ORIGINAL SOURCE:

(A) ORGANISM: ompF of E.coli

(ix) FEATURE:

15 (A) NAME/KEY: CDS

(B) LOCATION: 457..1545

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

| | AAAACTAATC | CGCATTCTTA | TTGCGGATTA | GTTTTTCTT | AGCTAATAGC | ACAATTTTCA | 60 |
|-----|------------|------------|------------|------------|------------|------------|------|
| | TACTATTTT | TGGCATTCTG | GATGTCTGAA | AGAAGATTTT | GTGCCAGGTC | GATAAAGTTT | 120 |
| 25 | CCATCAGAAA | CAAAATTTCC | GTTTAGTTAA | TTTAAATATA | AGGAAATCAT | ATAAATAGAT | 180 |
| | TAAAATTGCT | GTAAATATCA | TCACGTCTCT | ATGGAAATAT | GACGGTGTTC | ACAAAGTTCC | 240 |
| 30 | TTAAATTTA | CTTTTGGTTA | CATATTTTT | CTTTTTGAAA | CCAAATCTTT | ATCTTTGTAG | 300 |
| , 0 | CACTITCACG | GTAGCGAAAC | GTTAGTTTGA | ATGGAAAGAT | GCCTGCAGAC | ACATAAAGAC | ·360 |
| | ACCAAACTCT | CATCAATAGT | TCCGTAAATT | TTTATTGACA | GAACTTATTG | ACGGCAGTGG | 420 |
| | | | | | | | |

35 CAGGTGTCAT AAAAAAAACC ATGAGGGTAA TAAATA ATG ATG AAG CGC AAT ATT

1

Met Met Lys Arg Asn Ile

| WC | 99/49026 | |
|----|--|-----|
| | CTG GCA GTG ATC GTC CCT GCT CTG TTA GTA GCA GGT ACT GCA AAC GCT Leu Ala Val Ile Val Pro Ala Leu Leu Val Ala Gly Thr Ala Asn Ala | 522 |
| | 10 15 20 | |
| | AND CONTROL AND CITA GAT CTG TAC GGT AAA | 570 |
| 5 | GCA GAA ATC TAT AAC AAA GAT GGC AAC AAA GTA GAT CTG TAC GGT AAA | |
| | Ala Glu Ile Tyr Asn Lys Asp Gly Asn Lys Val Asp Leu Tyr Gly Lys 35 30 35 | |
| | 25 30 33 | |
| | GCT GTT GGT CTG CAT TAT TTT TCC AAG GGT AAC GGT GAA AAC AGT TAC | 618 |
| 10 | Ala Val Gly Leu His Tyr Phe Ser Lys Gly Asn Gly Glu Asn Ser Tyr | |
| | 40 45 50 | |
| | | |
| | GGT GGC AAT GGC GAC ATG ACC TAT GCC CGT CTT GGT TTT AAA GGG GAA | 666 |
| | Gly Gly Asn Gly Asp Met Thr Tyr Ala Arg Leu Gly Phe Lys Gly Glu | |
| 15 | 55 60 65 70 | |
| | TAL AGO COT TAL CCI CAG TCC GAA TAT AAC | 714 |
| | ACT CAA ATC AAT TCC GAT CTG ACC GGT TAT GGT CAG TGG GAA TAT AAC | |
| | Thr Gln Ile Asn Ser Asp Leu Thr Gly Tyr Gly Gln Trp Glu Tyr Asn 75 80 85 | |
| | 75 80 53 | |
| 20 | TTC CAG GGT AAC AAC TCT GAA GGC GCT GAC GCT CAA ACT GGT AAC AAA | 762 |
| | Phe Gln Gly Asn Asn Ser Glu Gly Ala Asp Ala Gln Thr Gly Asn Lys | |
| | 90 95 100 | |
| | | |
| 25 | ACG CGT CTG GCA TTC GCG GGT CTT AAA TAC GCT GAC GTT GGT TCT TTC | 810 |
| | Thr Arg Leu Ala Phe Ala Gly Leu Lys Tyr Ala Asp Val Gly Ser Phe | |
| | 105 110 115 | |
| | TAC ACC | 858 |
| | GAT TAC GGC CGT AAC TAC GGT GTG GTT TAT GAT GCA CTG GGT TAC ACC | 656 |
| 30 | Asp Tyr Gly Arg Asn Tyr Gly Val Val Tyr Asp Ala Leu Gly Tyr Thr | |
| ¥ | 120 125 130 | |
| | GAT ATG CTG CCA GAA TTT GGT GGT GAT ACT GCA TAC AGC GAT GAC TTC | 906 |
| | Asp Met Leu Pro Glu Phe Gly Gly Asp Thr Ala Tyr Ser Asp Asp Phe | |
| | 140 145 150 | |
| 35 | 135 | |
| | TTC GTT GGT CGT GTT GGC GGC GTT GCT ACC TAT CGT AAC TCC AAC TTC | 954 |
| | | |



| | Phe | Val | Gly | Arg | Val 155 | Gly | G1 y | Val | Ala | Thr 160 | Tyr | Arg | Asn | Ser | Asn 165 | Phe | |
|-----|-------|--------|-------|-------|---|-------|----------|-------|-------|------------|-----|-------|-----|-------|------------|-----|------|
| | П | GGT | CTG | GTT | GAT | GGC | CTG | AAC | ттс | GCT | GTT | CAG | TAC | CTG | GGT | AAA | 1002 |
| 5 | Phe | Gly | Leu | Val | Asp | Gly | Leu | Asn | Phe | Ala | Val | Gln | Tyr | Leu | Gly | Lys | |
| | | | | 170 | | | | | 175 | | | | | 180 | | | |
| | A A C | CAC | CCT | CVC | ۸CT | GC A | ՐԵՐ | CGT | TCT | AAC. | GGC | GAC | GGT | GTT | GGC | GGT | 1050 |
| | | | | | | | | | | | | Asp | | | | | |
| 10 | 7311 | Q10 | 185 | ,,,,, | • | | J | 190 | | | | • | 195 | | | | |
| | | | | | | | | | | | | | | | | | |
| | тст | ATC | AGC | TAC | GAA | TAC | GAA | GGC | Ш | GGT | ATC | GTT | GGT | GCT | TAT | GGT | 1098 |
| | Ser | Ιle | Ser | Tyr | Glu | Tyr | Glu | G1y | Phe | Gly | Пe | Val | Gly | Ala | Tyr | Gly | |
| | | 200 | | | | | 205 | | | | | 210 | | | | | |
| 15 | | | | | | | | | | CCT | C44 | ССТ | CTT | ccc | A A C | CCT | 1146 |
| | | | | | | | | | | | | CCT | | | | | 1140 |
| | | Ala | Asp | Arg | ınr | 220 | Leu | GIII | Giu | AIG | 225 | Pro | Leu | uiy | 7311 | 230 | |
| | 215 | | | | | 220 | | | | | LLU | | | | | | |
| 20 | AAA | AAA | GCT | GAA | CAG | TGG | GCT | ACT | GGT | CTG | AAG | TAC | GAC | GCG | AAC | AAC | 1194 |
| | Lys | Lys | Ala | Glu | Gln | Trp | Ala | Thr | Gly | Leu | Lys | Tyr | Asp | Ala | Asn | Asn | |
| | | | | | 235 | | | | | 240 | | | | | 245 | | |
| | | | | | | | | | | | | | CCT | 400 | 000 | ATC | 1242 |
| | | | | | | | | | | | | AAC | | | | | 1242 |
| 25 | Ile | Tyr | Leu | | | Asn | ıyr | ч | 255 | inr | Arg | Asn | АІа | 260 | | 116 | |
| | | | | 250 | | | | | 233 | | | | | 200 | | | |
| | ACT | AAT | AAA | ПТ | ACA | AAC | ACC | AGC | GGC | ттс | GCC | AAC | AAA | ACG | CAA | GAC | 1290 |
| | | | | | | | | | | | | Asn | | | | | |
| 30 | | | 265 | | | | | 270 | | | | | 275 | | | | |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | TCC | 1338 |
| | ۷a۱ | | | Val | Ala | Gln | | | Phe | Asp | Phe | | | ı Arç | Pro | Ser | |
| 2.5 | | 280 |) | | | | 285 | 1 | | | | 290 | 1 | | | | |
| 35 | ATC | י ביים | Γ ΤΔΓ | : Arr | : ΔΔ | י דרז | - ΔΔΔ | , GCF | . AAA | GAC | GT/ | A GAA | GG1 | ГАТС | GGT | GAT | 1386 |
| | AIC | , 401 | | | | | | | | | | _ | | | | | |

Ile Ala Tyr Thr Lys Ser Lys Ala Lys Asp Val Glu Gly Ile Gly Asp



| wo | 99/4 | 9026 | | | | | | | | | | | | | | | PCT/GB9 | 9 |
|-----|------|------|-------|------------|------------|------|------|------|------------|------------|------|------|--------------|------------|------------|-------|-----------------|---|
| | 295 | | | | | 300 | | | | | 305 | | | | | 310 | | |
| | | | | | | | | | | | | ACC | | | | | 1434 | |
| 5 | Val | Asp | Leu | Val | Asn 315 | Tyr | Phe | Glu | Val | G1y 320 | Ala | Thr | Tyr | Tyr | Phe 325 | Asn | | |
| | AAA | AAC | ATG | TCC | ACC | TAT | GTT | GAC | TAC | ATC | ATC | AAC | CAG | ATC | GAT | тст | 1482 | |
| | Lys | Asn | Met | Ser 330 | Thr | Tyr | Val | Asp | Tyr 335 | Ile | Ile | Asn | G1n | 11e 340 | Asp | Ser | | |
| 10 | | | | 0.70 | 000 | CTA | CCT | TCA | CAC | CAC | ۸۵۲ | GTT | CCT | GTG | CCT | ATC | 1530 | |
| | | | | | | | | | | | | Val | | | | | 1330 | |
| 15 | | | G1 n | | | TAG | CACA | CCT | СТТТ | GTTA | AA T | GCCG | 144 0 | A AC | AGGA | стт | 1585 | |
| 2.0 | GGT | CCTG | т. | Ш | TATA | сс т | TCCA | GAGC | A AT | CTCA | CGTC | TTG | CAAA | AAC . | AGCC | TGCGT | T 1645 | |
| 20 | ттс | ATCA | GTA . | ATAG | TTGG | AA T | ТТG | TAAA | т ст | CCCG | TTAC | CCT | GATA | GCG | GACT | тссст | T 1 70 5 | |
| | СТС | TAAC | CAT | AATG | GAAC | ст с | GTCA | TGTT | T GA | GAAC | ATTA | CCG | CCGC | TCC | TGCC | GACCC | G 1765 | |
| 25 | ATT | CTGG | GCC | TGGC | CGAT | CT G | ттс | GTGC | C GA | TGAA | CGTC | CCG | | | | | 1808 | |
| | (2) | INF | ORMA | TION | l FOR | SEC | ID | NO: | 6: | | | | | | | | | |

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 362 amino acids.

(B) TYPE: amino acid(D) TOPOLOGY: linear

35 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:



| | Met 1 | Me | et | Lys | Arg | Asn 5 | Ile | Leu | Ala | Val | Ile 10 | Val | Pro | Ala | Leu | Leu 15 | Val |
|----|-----------|-----|------------------|-----------|------------|-------------------|--------------|------------|------------|------------|------------|-----------|-----------|------------|------------|--------------|------------|
| 5 | Ala | G1 | ly | Thr | Ala 20 | Asn | Ala | Ala | Glu | Ile 25 | Tyr | Asn | Lys | Asp | Gly 30 | Asn | Lys |
| | Val | As | sp | Leu 35 | Tyr | Gly | Lys | Ala | Va1 40 | G1y | Leu | "His | Tyr | Phe 45 | Ser | Lys | Gly |
| 10 | Asn | | 1 <i>y</i> 50 | Glu | Asn | Ser | Tyr | G1 y 55 | G1 y | Asn | Gly | Asp | Met 60 | Thr | Tyr | Ala | Arg |
| | Leu 65 | | ly | Phe | Lys | Gly | G1u 70 | Thr | Gln | Ile | Asn | Ser 75 | Asp | Leu | Thr | Gly | Tyr 80 |
| 15 | Gly | G G | ln | Trp | Glu | Tyr 85 | | Phe | Gln | G1 y | Asn 90 | Asn | Ser | Glu | Gly | A1 a 95 | Asp |
| 20 | Ala | ı G | iln | Thr | Gly 100 | | Lys | Thr | Arg | Leu 105 | | Phe | Αla | Gly | Leu 110 | | Tyr |
| | Ala | a A | \sp | Val | | / Ser | • Phe | e Asp | Tyr 120 | | ⁄ Arç | j Asn | Tyr | Gly 125 | | Val | Tyr |
| 25 | Ası | | 41 a 130 | | (G1 | / Tyi | ~ Thr | • Asp | | : Leı | ı Pro | Glu | 140 | | / Gly | ⁄ Asp | Thr |
| | A1 14 | | Tyr | Sei | - Ası | o As _i | p Phe 150 | | e Val | l Gly | y Ang | g Val | | y Gl | y Val | Ala | Thr 160 |
| 30 | Ту | r | Arg |) Ası | n Se | r As 16 | | e Ph | e Gl | y Le | u Va 17 | | o G1; | y Le | u Ası | n∍Phe 175 | e Ala |

Val Gln Tyr Leu Gly Lys Asn Glu Arg Asp Thr Ala Arg Arg Ser Asn 180 185 190

Gly Asp Gly Val Gly Gly Ser Ile Ser Tyr Glu Tyr Glu Gly Phe Gly



195 200 205

Ile Val Gly Ala Tyr Gly Ala Ala Asp Arg Thr Asn Leu Gln Glu Ala 210 215 220

- Gln Pro Leu Gly Asn Gly Lys Lys Ala Glu Gln Trp Ala Thr Gly Leu 225 230 235 240
- Lys Tyr Asp Ala Asn Asn Ile Tyr Leu Ala Ala Asn Tyr Gly Glu Thr

 245 250 255
 - Arg Asn Ala Thr Pro Ile Thr Asn Lys Phe Thr Asn Thr Ser Gly Phe
 260 265 270
- 15 Ala Asn Lys Thr Gln Asp Val Leu Leu Val Ala Gln Tyr Gln Phe Asp 275 280 285
 - Phe Gly Leu Arg Pro Ser Ile Ala Tyr Thr Lys Ser Lys Ala Lys Asp 290 295 300
- Val Glu Gly Ile Gly Asp Val Asp Leu Val Asn Tyr Phe Glu Val Gly 305 310 315 320
- Ala Thr Tyr Tyr Phe Asn Lys Asn Met Ser Thr Tyr Val Asp Tyr Ile
 25 325 330 335
 - Ile Asn Gln Ile Asp Ser Asp Asn Lys Leu Gly Val Gly Ser Asp Asp 340 345 350
- 30 Thr Val Ala Val Gly Ile Val Tyr Gln Phe * 355 360